The Cochrane Library

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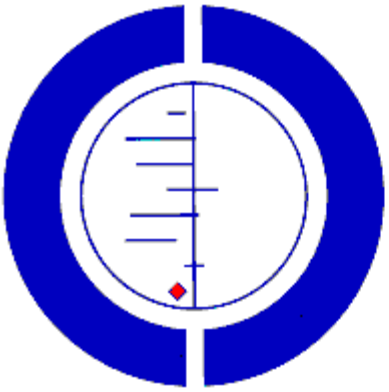

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The best single source of reliable evidence about the effects of health care

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This guide was first produced for the University of Cambridge Programme for Industry course “Epidemiology and the Health Service”. Subsequently it was adapted as supporting material for a training course delivered to librarians in the Anglia and Oxford Region. This edition updates the guide for the Cochrane Library disk issue 4, 1998. The task of keeping the guide up to date has now been taken over by Ruth Frankish at the CRD. Please address any queries about the quide to her.

This guide can be downloaded as a Word 6.0 document from the CRD web pages , together with a Powerpoint slide show containing all the graphics in the guide:

We make no commitment to keep the guide up to date with future software releases. The guide forms a basic introduction for those new to the Cochrane Library - it does not attempt to detail every feature of the Cochrane Library.

1. Systematic Reviews and the Cochrane Collaboration

Outcomes

After finishing this section you should be able to describe:

- *what a systematic review is and why they are important to decisions relating to healthcare.*
- *the role of the Cochrane Centre within the NHS R&D information strategy*
- *the nature and organisation of the Cochrane collaboration.*

1.1 Systematic Reviews

A **review** is any attempt to synthesise the results and conclusions of two or more publications on a given topic.

A **systematic review** is a review that strives comprehensively to identify and synthesise all the literature on a given topic (sometimes called an overview). The unit of analysis is the primary study and the same scientific principles and rigour apply as for any study. If a review does not state clearly whether and how all relevant studies were identified and synthesised it is not a systematic review.

Meta-analysis is a statistical technique for assembling the results of several studies in a review into a single numerical estimate.

Many reviews are not systematic but are still valuable and helpful so long as the reader is aware and takes account of the fact. A systematic review can be performed on any type of scientific evidence, both quantitative and qualitative. Consequently not all systematic reviews are meta-analyses. However a meta-analysis that is not a systematic review is likely to be highly biased and should be used with extreme caution or not used at all.

Systematic reviews are an increasingly important source of evidence about the effects of health care because:

- They help decision makers to cope with the sheer volume of literature by summarising it
- They provide 'new' information which may not be apparent from individual studies where the effects under investigation are small
- The quality of systematic reviews is fast improving due to the efforts of the Cochrane Collaboration and the NHS Centre for Reviews and Dissemination

They key characteristics of a systematic review are:

- Clearly stated title and objectives for the review
- Comprehensive strategy to search for studies that address the objectives of the review (relevant studies) to include unpublished as well as published studies
- Explicit and justified criteria for the inclusion or exclusion of any study
- Comprehensive list of all studies identified
- Clear presentation of the characteristics of each study included and an analysis of methodological quality
- Comprehensive list of all studies excluded and justification for exclusion

- Clear analysis of the results of the eligible studies using statistical synthesis of data (meta-analysis) if appropriate and possible
- Sensitivity analyses of the synthesised data if appropriate and possible
- Structured report of the review clearly stating the aims, describing the methods and materials and reporting the results

A systematic review should be as well written as possible and include as much of the above information as the publication medium allows. Paper based scientific journals tend to limit the number of tables and figures which emphasises the need for clear and concise writing. The Cochrane Database of Systematic Reviews allows all of the above information to be presented in a structured way which ensures the highest quality possible.

1.2 Evidence about clinical effectiveness

Evidence about the clinical effectiveness of health care interventions is becoming increasingly more widely sought and applied by both NHS health care purchasers and practitioners alike. The Cochrane Collaboration and the NHS Centre for Reviews and Dissemination (see below) are concerned solely with evidence from good quality reviews and systematic reviews and their output is being increasingly used. However, it is important not to dismiss primary studies as they are more likely to be the only source of (scientific) evidence in most areas of health care than systematic reviews. A powerful and well conducted single research study can easily provide sufficient evidence to preclude the need for further studies and thus any form of review. But, even if a primary study is not particularly powerful it can still be used as evidence about clinical effectiveness in the absence of any alternative or until further studies or systematic reviews have been conducted. How strong that evidence is a function of the study design and the sample size. The following table provides a ready guide to the different types of evidence about clinical effectiveness and their relative strengths.

Type and Strength of Evidence	
I	Strong evidence from at least one systematic review of well designed RCTs
II	Strong evidence from at least one properly designed RCT of appropriate size
III	Evidence from well designed trials without randomisation: single group pre-post, cohort, time series or matched case-controlled studies
IV	Evidence from well designed non-experimental studies from more than one centre or research group
V	Opinions of respected authorities, based on clinical evidence, descriptive studies or reports of expert committees
VI	Someone once told me

In the table above type I evidence is the strongest, type VI the weakest. The strength of the evidence is related to the degree to which bias and confounding factors are controlled. By definition this means that quantitative study designs provide the strongest evidence because they provide the best means of controlling for bias but only if the sample size is large enough and appropriate to control for random effects. This does not mean that the weaker types of evidence in the table are not reliable but simply that it is more difficult to control for bias and random effects. There are many instances where quantitative forms of study design are either not possible or are inappropriate or are even unethical. This could be due to the limited availability of subjects with a particular condition, the need to directly observe subjects to acquire data, the unavailability of any alternative treatment (which would make the withholding of treatment from the control group unethical) or the size and nature of the effect under observation.

Studies which show dramatic effects require less control for bias and random effects than those which show only small effects. Therefore the most appropriate type of study design is also dependent on the size of the effect under investigation as shown in the table below. In the case of the first use of penicillin for severe infections the patients either died or survived, the effect being so dramatic that observation of single patients provided sufficient power to clearly demonstrate effectiveness. At the opposite extreme the effect of steroids on the maturation of the lungs of preterm babies and their survival is a small effect that can only be measured in terms of percentage improvements in outcome in a population as opposed to an individual effect for each mother treated. Therefore the most powerful form evidence is needed to control for bias and random effects in order to be able to show clear benefit.

Study method	**Example**	**Size of the effect**
observation in single patients	penicillin for severe infections	++++
observation in groups of patients	smoking and lung cancer	+++
randomised cotrolled trials	aspirin and streptokinase for heart attacks	++
systematic reviews	steroids for women expected to deliver prematurely	+

The two tables above should be used only as a rough guide to whether a particular form of study is appropriate and likely to yield reliable and useful evidence of clinical effectiveness. It should never be forgotten that research studies tend to produce results that may not be relevant to a particular patient or setting and that the clinical experience of each practitioner is also a powerful form of evidence in applying the results of research in practice.

1.3 NHS R&D Information Strategy

The NHS R&D Information Systems Strategy (ISS) has been designed to provide a framework for the various information systems which are needed to support the NHS R&D programme. There are three key elements to the strategy; the UK Cochrane Centre, the NHS Centre for Reviews and Dissemination and the NHS R&D National Research Register.

1.4 UK Cochrane Centre

The UK Cochrane Centre (UKCC) was established at the end of 1992 to facilitate and coordinate the preparation and maintenance of systematic reviews of randomized controlled trials of health care. During its initial period of funding (1992-1995), the Centre's objectives included a number of activities intended to help establish the Cochrane Collaboration (see section 1.7,) and it is now one of fifteen Cochrane Centres around the world which provide the infrastructure for coordinating the Cochrane Collaboration. Following the external review which led to approval for its second period of funding (1995-1999), the Centre has concentrated on fulfilling its national role within the Collaboration - to support people within the UK who are contributing to the Collaboration's work. In addition, the UKCC is the reference Cochrane Centre for people living in certain countries in Central Europe and the Middle East who wish to contribute to the Collaboration. The director of the UKCC is Dr. Iain Chalmers

OBJECTIVES
To support people in the UK who are helping to prepare and maintain Cochrane Reviews through:

- General support and infrastructure for preparing and maintaining Cochrane reviews.
- Training for those preparing and maintaining Cochrane reviews.
- Supporting professionals allied to medicine and consumers helping to prepare and maintain Cochrane reviews.
- Support in identifying and registering relevant controlled trials.
- To further the international development of the Cochrane Collaboration.

1.5 NHS Centre for Reviews and Dissemination

A reviews facility has been established to provide the NHS with important information on the effectiveness of treatments and the delivery and organisation of healthcare. The NHS Centre for Reviews and Dissemination (CRD) was established at the end of 1993 at the University of York, and the current director is Professor Jos Kleijnen. CRD conducts reviews in areas prioritised by the NHS HTA programme and Effective Healthcare Bulletin prioritisation process. It also undertakes reviews in its own right and commissions and supports experts to undertake reviews. The facility ensures that reviews meet, and are seen to meet, explicit quality criteria. Reviews take account of all research relevant to their area, including work funded in this country by organisations other than the NHS, and work undertaken overseas. Close co-operation is maintained with the UK Cochrane Centre and with others having interests in this work.

R&D findings are unlikely to influence NHS decision-makers if the form in which they are disseminated is inappropriate to the needs of users, which vary. CRD has an integral dissemination facility providing the specialist communications and editorial skills required to produce user-friendly materials. It aims to ensure the materials reach those NHS decision-makers who need them.

CRD also provides an enquiry-based service for health care professionals, purchasers and providers, information providers, health service researchers and consumer organisations. This service provides information on reviews of the effectiveness and cost-effectiveness of healthcare interventions, and referrals to appropriate sources of information.

The objectives of CRD are:

- to carry out and commission reviews and updates of research findings about the effectiveness and cost-effectiveness of health care
- to maintain and update an international database of quality assessed research reviews
- to contribute to the improvement of research reviews by preparing good practice guidelines and training material, and researching into the methodology of reviewing
- to disseminate research-based information effectively in a targeted way to the relevant professionals in the NHS and to consumers of its services
- to support activities which contribute to knowledge of those factors which influence practitioners' behaviour.

CRD produces and disseminates the well-known *Effective Health Care Bulletins* and *Effectiveness Matters* as well as guidelines on how to conduct systematic reviews.

Up to date information on CRD activities and reviews can be obtained from their web site at:
http://www.york.ac.uk/inst/crd/ from where it is also possible to search the free databases DARE and NHS Economic Evaluation Database.

1.6 NHS R&D National Research Register

A national register of research and development in the NHS is being established. The register will identify on-going research and help to identify forthcoming research findings thus counteracting delays in publication and aiding identification of unpublished research. As such the register will be a unique resource for both the health services and biomedical research community and those concerned with health care decision making.

The database currently holds 6000+ projects (as at October 1998), comprising largely R&D projects funded directly by the NHS R&D Levy through the National Priority Programmes, HTA programme and Regional funding schemes and also the Department of Health Priority Research Programme.

The objective of the NRR is to provide:

- a tool to support efficient research management, by identifying unwanted duplication of research projects;
- a decision-support tool for those commissioning new research or using existing research;
- a basis for accounting for expenditure on research
- an input to research overviews

The NRR also includes other products:

- Register of Registers - information about other registers of similar R&D project information
- MRC Clinical Trials Directory - information about clinical trials in receipt of an MRC grant
- NHS CRD Reviews in Progress register
- Other research registers

Work on developing the NRR is taken forward by a Project Board and Project Team which has consulted widely with the NHS, the library and information science community and the medical research community.

Expanding coverage
The data collection strategy has been extensively reviewedand health care providers in receipt of R&D levy support funding (Culyer funding) will begin contributing to the NRR in the coming year 1998/9, submitting registers of R&D taking place in the providers. At this time it is not possible to predict the volume of records which this will generate, but it is likely to expand the NRR to 20-30,000+ records in due course. The data collection strategy will be further developed to draw in other sources of "research in progress" information.

New retrieval software
The project team have been working with Update Software, the producers of the Cochrane Library interface, and potential users of the NRR to develop an much improved retrieval interface, and recently a prototype CD-ROM product has been circulated. Until that point, access to the NRR was restricted to the NHS Executive Regional Offices, but from the issue of the prototype, access will be at provider and health authority level.

A further issue of the NRR appeared in Summer 1998, which will be followed by the next issue in winter 1998, which will contain substantial numbers of Culyer generated records. A publication strategy is being developed which will explore other methods of dissemination such as Internet and NHSnet.

Further information on the NRR can be obtained from:

Sam Brown, NHS Executive Headquarters, RD3
Quarry House Room GW59
Quarry Hill

Leeds LS2 7UE

1.7 The Cochrane collaboration

In an influential book published more than twenty years ago[1], Archie Cochrane drew attention to our great collective ignorance about the effects of health care, and explained how evidence from randomized controlled trials (RCTs) could help us to use resources more rationally. He recognized that people who wanted to take more informed decisions about health care did not have ready access to reliable reviews of the available evidence. In 1979, he wrote: "It is surely a great criticism of our profession that we have not organised a critical summary, by specialty or subspecialty, adapted periodically, of all relevant randomized controlled trials" [2].

The Cochrane Collaboration has evolved in response to this challenge. Contributors in many countries and specialties are preparing and maintaining systematic reviews of RCTs, and reviews of other evidence when appropriate. This international endeavour aims to ensure that, in due course, all areas of health care which have been evaluated using RCTs will be covered. The reviews prepared and maintained by the Collaboration are disseminated using electronic media through The Cochrane Database of Systematic Reviews.

Mission Statement
The Cochrane Collaboration is an international organisation that aims to help people make well-informed decisions about healthcare by preparing, maintaining and promoting the accessibility of systematic reviews of the effects of healthcare interventions.

Principles
The Cochrane Collaboration's work is based on eight key principles:

- Collaboration...by internally and externally fostering good communications, open decision-making and teamwork.
- Building on the enthusiasm of individuals...by involving and supporting people of different skills and backgrounds.
- Avoiding duplication...by good management and co-ordination to maximise economy of effort.
- Minimising bias...through a variety of approaches such as scientific rigour, ensuring broad participation, and avoiding conflicts of interest.
- Keeping up to date...by a commitment to ensure that Cochrane Reviews are maintained through identification and incorporation of new evidence.
- Striving for relevance...by promoting the assessment of healthcare interventions using outcomes that matter to people making choices in health care.
- Promoting access...by wide dissemination of the outputs of the Collaboration, taking advantage of strategic alliances, and by promoting appropriate prices, content and media to meet the needs of users worldwide.
- Ensuring quality...by being open and responsive to criticism, applying advances in methodology, and developing systems for quality improvement.

1.8 How the Cochrane Collaboration Works

The Cochrane Collaboration is an international network of individuals helping to prepare, maintain and disseminate systematic reviews (Cochrane Reviews) of the effects of health care. In general, these reviews tend to be based on the results of randomised controlled trials (RCTs), but information derived from research using other designs is used when appropriate. To explain how the Collaboration works, let's consider how Cochrane Reviews are prepared, maintained and disseminated for public and professional use.

It all starts with individuals - health professionals, consumers and researchers - with interests in a particular health problem or group of problems: what is the best treatment for stroke and how might

we reduce the risk of its recurrence? How should we minimise the harm from malaria in pregnant women living in areas of the world where the disease is endemic? How can people who want to give up smoking be helped?

Some of these individuals come to learn of the Collaboration. This may happen through the Collaboration's introductory brochure, its Handbook, or electronically published Cochrane Reviews; through information obtained from people at their nearest Cochrane centre or others contributing to the Collaboration; or in one of many other ways. Among these individuals, some decide that the objectives and framework of the Collaboration provide an important way of addressing the health problem in which they are interested, and that they would like to explore how they might contribute to its work. By requesting their local Cochrane centre to arrange for their names, contact details and interests to be entered on the Collaboration's directory, they make their interests known to the Collaboration as a whole.

Staff at the Cochrane centres try to ensure that people who have registered interests with the Collaboration in this way are placed in contact with other like-minded individuals involved in or in touch with the Collaboration. After a varying amount of time, and with guidance from Cochrane centre staff, one or more of these individuals will volunteer to act as a facilitator to establish a network of individuals who share an interest in a particular health problem or group of problems. If exchange of information among individuals in the network suggests that they might be able to work together collaboratively, one or more of them, liaising closely with the staff of one or more Cochrane centres, convenes an exploratory meeting of all those registered with the Collaboration as having an interest in the health problem concerned.

At that or subsequent exploratory meetings, a group of individuals agree that they would like to work together, and that they are prepared to assume responsibility, for the foreseeable future, for preparing and maintaining systematic reviews of strategies to prevent and treat the health problem or problems in which they share an interest. In close consultation with the nearest Cochrane Centre (to maximise efficiency and minimise unnecessary duplication of effort), members of the group prepare a plan for how they wish to organise themselves. This plan defines the scope of the group; describes who will have particular responsibility for planning and monitoring its work (editors, including one who will act as the co-ordinating editor); how the group will identify and assemble all the relevant studies in a specialised register; and who will take responsibility for preparing and maintaining which reviews (Cochrane Reviewers). Every group will appoint an individual to organise and manage the day-to-day activities of the group (an administrator), who will be based at the same place as the co-ordinating editor.

Together with a supporting letter from the reference Cochrane centre, the group's plan is submitted to a panel of individuals representing all of the various elements of the Cochrane Collaboration (the Steering Group). If the plan is approved, the group becomes registered as a Collaborative Review Group (CRG). This process ensures that CRGs are both multidisciplinary and international - indeed, it is a requirement of the Collaboration that they should be.

Members of the CRG now get down to work! Finding all of the relevant evidence is a daunting task, since existing bibliographic databases not only exclude most unpublished evidence, but even fail to identify many of the relevant published reports. The Cochrane Collaboration helps CRGs to meet this challenge in several different ways. First, it has developed an efficient search strategy for MEDLINE, and it is working with the US National Library of Medicine to improve the identification of both old and newly published trials through MEDLINE. Second, through a database maintained at the Baltimore Cochrane Centre, the CRG can identify those journals that have already been or are currently being hand searched for all trials. (This database is available via the web http://www.cochrane.org/

The work of hand searching journals is shared among CRGs, each of which is expected to search - for all RCTs - the specialist publications relevant to the specific health problems within its scope. Cochrane centres are responsible for searching general health care publications. The task of identifying RCTs is also being addressed by other collections of individuals contributing to the Cochrane Collaboration, who, rather than focusing on health problems, have coalesced around

dimensions of health care - settings of care (for example, primary health care), classes of intervention (for example, vaccines), or kinds of health service user (for example, elderly people). These collections of contributors, who organise searches of their specialist literature, are known within the Collaboration as fields.

Other challenging tasks confront the members of the CRG as they assemble, appraise, and synthesise the relevant evidence into Cochrane Reviews. Reviewers need to develop their individual protocols for Cochrane Reviews, commit themselves to a timetable for preparing them, assess individual trials for their relevance and reliability (often necessitating communication with the investigators), synthesise their results, and prepare the structured report that constitutes the Cochrane Review. The editorial team, centred round the administrator, will have to develop strategies for co-ordinating and facilitating these processes.

Members of CRGs are helped to tackle these tasks by instructional documents (including sections of the Handbook) and workshops (organised by Cochrane centres and CRGs), both of which are based (whenever possible) on the results of empirical research. Such methodological research is the focus of individuals who have come together in methods working groups which are tackling a wide variety of issues, ranging from prospective registration of RCTs to dissemination and quality assurance of Cochrane Reviews.

Software has also been developed by the Cochrane Collaboration to help CRGs do their work. CRGs make particular use of two software packages. The first - Review Manager - provides both an organisational and analytic framework for assembling Cochrane Reviews in electronic format; the second - Module Manager - enables administrators and editors to assemble up-to-date reviews prepared by the members of their CRG, as well as information about the CRG itself, for example, the scope of its work, and the strategy used to assemble a specialised register of relevant studies.

This collection of Cochrane Reviews and information about the CRG, known as a module, is the CRG's principal contribution to the Cochrane Collaboration. Together with modules from all the other CRGs, it contributes to the Parent Database of Cochrane Reviews. It is from this continuously updated Parent Database that Cochrane Reviews (and titles and protocols of those reviews that are in the process of being prepared) are disseminated. Dissemination takes place through the Cochrane Library, which is updated quarterly.

1.9 Cochrane Centres

Cochrane centres share a responsibility for helping to co-ordinate and support the Cochrane Collaboration. The responsibilities include:

- maintaining a directory of people contributing to the Collaboration, with information about their individual responsibilities
- maintaining a directory of people who have expressed interest in contributing to the Collaboration, with information about their specific interests
- helping to establish and support collaborative review groups by:
    - fostering international collaboration among people with similar interests
    - participating in exploratory discussions and meetings
    - helping to organise workshops, and
    - in other ways, facilitating collaboration
- co-ordinating hand searches of the general medical journals and monitoring and assisting review groups searching specialist literature published within the geographical area serviced by the Centre

- co-ordinating the Collaboration's contributions to the creation and maintenance of an international register of completed and ongoing RCTs, thus facilitating the first phase of data collection for reviewers
- preparing and developing protocols and software - compiled in successive editions of the Collaboration's guidelines - to systematise and facilitate the preparation and updating of systematic reviews
- making arrangements for efficient electronic transfer of reviews between reviewers and CRG administrators and editors; between CRG administrators and the parent database of Cochrane Reviews; and between the parent database and The Cochrane Database of Systematic Reviews developing policies and setting standards to maximise the reliability of information disseminated through The Cochrane Electronic Libraries.
- promoting and undertaking research to improve the quality of systematic reviews
- exploring ways of helping the public, health service providers and purchasers, policy makers and the press to make full use of Cochrane Reviews, The Cochrane Electronic Library, organising workshops, seminars and Colloquia to support and guide the development of the Cochrane Collaboration

The Cochrane centres are NOT directly responsible for preparing and maintaining systematic reviews. This is the responsibility of collaborative review groups which also maintain registers of systematic reviews currently being prepared or planned, so that unnecessary duplication of effort can be minimised and collaboration promoted. In addition to the shared responsibilities mentioned above, some centres have specific interests and tasks. These are described in the information provided for the individual centres.

[1] Cochrane, A.L. “Effectiveness and Efficiency: random reflections on Health Services.” London, Nuffield Provincial Hospitals Trust, 1972 (Reprinted in 1989 in association with the BMJ)

[2] Cochrane, A.L. “1931-1971: a critical review, with particular reference to the medical profession.” In: Medicines for the year 2000. London, Office of Health Economics, 1979, 1-11